REMARKS

Applicants appreciate the thorough examination of the present application that is reflected in the final Official Action of July 25, 2007 and the Examiner's thoughtful remarks in the Advisory Action of October 31, 2007. In response, the present RCE and Amendment are being filed. The present RCE and Amendment are being filed for three purposes: (1) to allow entry of the present Amendment, which includes the amendments and arguments that were made in Applicants' unentered Amendment After Final Action of October 15, 2007; (2) to add additional analysis based upon the Examiner's remarks in the Advisory Action; and (3) to further amend the dependent claims and add dependent claims that further highlight patentable distinctions over U.S. Patent Application Publication US 2003/0083716 to Nicolelis et al. in view of U.S. Patent 6,366,813 to DiLorenzo, taken together or in combination with the other secondary references. Applicants respectfully request a telephone interview with the Examiner when the Examiner is ready to examine the present RCE, to review the arguments set forth herein and to advance the application to allowance.

The Independent Claims Are Patentable Over Nicolelis et al. In View of DiLorenzo

Independent Claims 1, 19 and 30 stand rejected under 35 USC §103(a) over Nicolelis et al. in view of DiLorenzo. These claims are structural, method and functional analogs of one another. Accordingly, for the sake of brevity, only Claim 1 will be analyzed. Independent Claim 1 recites:

> 1. A system for detecting neural events comprising:
> a neural event electrode interface that is configured to communicate with electrodes that capture electrical signals that are associated with at least one neuron;
> a neural event waveform processor that is configured to extract single neuron action potentials with waveforms that exceed 500 Hz from the electrical signals; and
> a wireless transmitter that is configured to wirelessly transmit the single neuron action potentials with waveforms that exceed 500 Hz that are extracted from the electrical signals. (Emphasis added.)

The final Official Action concedes at Page 2 that Nicolelis et al. does not disclose the extracted neural events as being single neuron action potentials having a frequency greater than 500 Hz as recited in Claim 1, but cites DiLorenzo as supplying the missing teaching.

Assume for the sake of argument that the cited passages of DiLorenzo describe the claimed "waveforms that exceed 500 Hz". Applicants respectfully submit, however, that substituting a waveform that exceeds 500 Hz into Nicolelis et al. would destroy the operability thereof. In particular, Nicolelis et al. is directed to an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*, as noted by the Nicolelis et al. title. Consistent with Nicolelis et al.'s object to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*, Nicolelis et al. specifically filters out waveforms that are not related to epileptic seizures. In particular, as described for example in Paragraph [0173] of Nicolelis et al.:

> In an example of a type of data analysis that can be performed, field potential traces can first be band-pass filtered at 5-30 Hz. A sliding window (e.g., a 1 sec window with a 0.5 sec overlap) can then be used to quantify the activity of the absolute values of the field potential traces. (Emphasis added.)

Applicants respectfully submit that if waveforms that exceed 500 Hz were substituted from DiLorenzo into Nicolelis et al., the operability of Nicolelis et al. would be destroyed, because brainwave field potential traces are monitored at frequencies between 5-30 Hz, which is more than an order of magnitude less than the frequencies being used by DiLorenzo. Accordingly, if DiLorenzo's filter was substituted into Nicolelis et al., Nicolelis et al. would appear to be inoperable.

Stated differently, Nicolelis et al.'s *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*, with its bandpass filter at 5-30 Hz, teaches away from the substitution of waveforms that exceed 500 Hz. As recently noted by the U.S. Supreme Court in *KSR International Co. v. Teleflex Inc., et al.* (550 U.S. 1, 12 (2007)), when the prior art teaches away from combining certain known elements, discovery of successful means of combining them is more likely to be non-obvious.

Applicants do not claim to have invented waveforms that exceed 500 Hz. In fact, Applicants admit that filters that pass waveforms greater than 500 Hz exist independently, as exemplified by DiLorenzo. However, the U.S. Supreme Court also recently noted that a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *Id.* at 14.

For at least these reasons, Claims 1, 19 and 30 are unobvious over Nicolelis et al. in combination with DiLorenzo and/or any other reference that teaches the use of signals with waveforms that exceed 500 Hz. All of the pending claims are therefore in condition for allowance for at least these reasons.

In response to these arguments, the Advisory Action stated that the example provided above from Nicolelis et al. Paragraph [0173] is but one example of the waveforms and filtering associated with Nicolelis et al., but is not limiting:

> ...Applicant has argued that extracting action potentials with waveforms exceeding 500 Hz would destroy the operability of Nicolelis (US 2003/0083716) because of an example of band-pass filtering. This particular example is one of several examples of waveforms and filtering associated with Nicolelis, and is in no way limiting - for instance, paragraph [0210] cites an entirely different band -pass [sic] filter range example, as well as paragraph [0133], which describes a range of notch filter wavelengths. Nicolelis does not disclose any limits to waveforms that may be monitored as part of the system, and does not teach away from monitoring wavelengths of any pa rticular [sic] frequency, because Applicant has merely cited a non-limiting example. Applicant's arguments are not persuasive

The Examiner is absolutely correct that Applicants only cited one example from Nicolelis et al., and that many other examples are provided in Nicolelis et al. However, every example in Nicolelis et al. is limited to frequencies well below 500 Hz, whereas the independent claims all recite waveforms that exceed 500 Hz.

Thus, Paragraph [0210] of Nicolelis et al. (cited in the Advisory Action) states:

> **[0210]** Field potential recordings from VPM thalamus and SI cortex were made using chronically implanted microwires (Nicolelis et al.,(1997) *Neuron* 18: 529-537). Field potentials were collected using a GRASS Model 15 amplifier and stored on a personal computer. Signals were collected at a sampling rate of 512 Hz and band pass filtered during collection at 1-100 Hz. During each recording session, 16 field potential channels were recorded, 8 from each area from which recordings were made in a given rat (either VPM and SI, or SI left and SI right). In addition, one channel was recorded for each nerve cuff being stimulated (unilateral or bilateral stimulation) to indicate when stimulation occurred. During experiments, animals were awake and allowed to move freely in a 30 cm×30 cm recording chamber. (Emphasis added.)

Moreover, Paragraph [0133] states:

> **[0133]** In one embodiment, a band-pass filter module of an automatic seizure detector can operate as a pre-filter to filter out frequency components of a signal that are extraneous to or could interfere with seizure detection. Such a filter can be applied in the present invention as a band-pass filter, with upper and lower cut-off values. A band-pass filter can be adapted to attenuate any frequency component of the signal that does not fall between these two values. Thus, frequencies, such as 60 Hz oscillations from nearby electrical devices, which could interfere with seizure detection, can be filtered out, whereas signal frequencies

> associated with a seizure will remain in the signal. This process generally makes the voltage signal from an electrode more representative of seizure activity, during the seizure detection process. Thus, a band-pass filter of the present invention preferably comprises a notch filter at 30 Hz, 60 Hz 90 Hz or another desired frequency. (Emphasis added.)

Again, frequencies well below 500 Hz are described. A similar description may be found in Paragraph [0028] of Nicolelis et al.

Applicants also note that Paragraphs [0211] and [0212] of Nicolelis et al. describe stimulation frequencies as high as 333 Hz, but also clearly describe field potential trace extraction at 5-30 Hz at Paragraph [0215]. Accordingly, the Examiner is correct that Nicolelis et al. includes many examples of band-pass and notch filter ranges. However, all of these ranges are less than 500 Hz and, in fact, are less than 100 Hz, whereas the independent claims recite the use of signals with waveforms that exceed 500 Hz. Accordingly, the Examiner's analysis in the Advisory Action actually reinforces the unobviousness of the independent claims. All of the pending claims therefore are in condition for allowance for at least these additional reasons.

Independent Claims 8 and 9 Are Separately Patentable

As noted above, Claims 8 and 9 have been rewritten in independent form. These claims are patentable at least for the same reasons that were described above in connection with Claim 1. Moreover, Claims 8 and 9 recite that the neural stimulation waveforms are provided to the neural event electrode interface so as to provide the neural stimulation waveforms to the electrodes. Thus, in Claims 8 and 9, the same electrodes are used to capture the electrical signals that are associated with at least one neuron and to stimulate the neuron itself, so that they operate in a bidirectional manner. In sharp contrast, in Nicolelis et al., different sets of electrodes **22** and **20** are used to capture the electrical signals and provide stimulation, respectively. The use of different electrodes is consistent with Nicolelis et al.'s desire to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*, and it would not be obvious from Nicolelis et al. to use the same electrodes for capturing signals and for stimulation.

Applicants wish to note that similar arguments were made for Claims 8 and 9 (in dependent form) in Applicants' earlier Amendment of May 16, 2007. Yet, neither the final Official Action nor the Advisory Action addressed these persuasive arguments. Claims 8 and

9 have now been rewritten in independent form to more directly bring these claims to the Examiner's attention. Should the Examiner persist in the rejection of these claims, the Examiner is respectfully requested to address how Nicolelis et al.'s different sets of electrodes **22** and **20** would render Claims 8 and 9 obvious.

Finally, Applicants also wish to note that although Claims 8 and 9 have not been rejected in view of DiLorenzo, DiLorenzo also does not supply the missing teachings. In particular, referring to DiLorenzo Figure 2, electrode arrays **50** and **51** are used to capture EMG and EEG signals, and a separate intracranial stimulating electrode array **37** is used to stimulate. Accordingly, even DiLorenzo teaches away from the recitations of Claims 8 and 9.

Many of the Dependent Claims Are Separately Patentable

Finally, Applicants also wish to highlight other dependent claims that are separately patentable. Neither the final Official Action nor the Advisory Action addressed any of the analysis that was provided earlier.

In particular, Claim 5 recites that the neural event waveform processor is further configured to identify a neuron that is responsible for the single neuron action potential at frequencies that exceed 500 Hz. In rejecting Claim 5, the Examiner cites Paragraphs [0052] and [0053] of Nicolelis et al. However, these paragraphs do not provide any description or suggestion of identifying an individual neuron, nor would there appear to be any need to identify an individual neuron in order to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*. Accordingly, Claim 5 is independently patentable.

Claim 7 has been amended extensively to highlight the patentable recitations thereof. In particular, Claim 7 now recites:

> 7. A system according to Claim 1 further comprising a wireless receiver that is configured to wirelessly receive instructions for configuring the neural event waveform processor to use a selected category of algorithms to extract the single neuron action potentials with waveforms that exceed 500 Hz, and to provide the instructions to use the selected category of algorithms to extract the single neuron action potentials with waveforms that exceed 500 Hz to the neural event waveform processor, wherein the neural event waveform processor is configured to use the selected category of algorithms to extract the single

> neuron action potentials with waveforms that exceed 500 Hz. (Emphasis added.)

Support for these claim amendments may be found, for example, at Pages 8-10 of the present application. Applicants respectfully submit that neither Nicolelis et al. nor DiLorenzo describes or suggests the ability to configure the neural event waveform processor to use a selected category of algorithms to extract the single neuron action potentials with waveforms that exceed 500 Hz. In particular, although in Nicolelis et al. various threshold parameters may be changed for the detection of neural and muscular activity consistent with a seizure, there is no disclosure or suggestion of changing the category of the algorithm that is used. Nor would changing the category of algorithm be consistent with Nicolelis et al.'s desire to provide a specialized detector that is used to stimulate the brain to control epileptic seizures. In sharp contrast, as noted at Page 10, lines 6-13 of the present application:

> As has been described, the wireless radio frequency transceiver (RF) **4** may be bi-directional and capable of both sending the neural data to a freestanding processor and receiving instructions regarding how to extract data of a particular type. For instance, it may be desirable for the researcher to be able to change the algorithms and assessment programs implemented by the DSP **2** so that different types of neural activity information can be collected or the same types of information can be collected more accurately—without having to adjust the WINE device by physically disconnecting it from the subject.

Accordingly, Claim 7 is independently patentable. Similar analysis applies to Claims 23, 37, 38 and 39.

Claim 14 is also independently patentable because Claim 14 recites that the electrical signals that are associated with the at least one neuron are generated by an *in vitro* sample. Clearly *in vitro* use would not apply to an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*. Nor would it be obvious to modify Nicolelis et al.'s *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"* to provide *in vitro* use, notwithstanding known analysis of signals from *in vitro* samples as exemplified, for example, by U.S. Patent 6,665,562 to Gluckman et al. Accordingly, Claim 14 is independently patentable. Similar analysis applies to method Claim 26.

Claim 17 is also independently patentable, because Claim 17 recites further processing of the single neuron action potentials with waveforms that exceed 500 Hz at a base station. Further processing at a base station does not appear to be described or suggested in Nicolelis et al. and, indeed, further processing would not appear to be needed in order to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*. Accordingly, Claim 17 is independently patentable.

Claim 18 also is independently patentable. In particular, Claim 18 recites:

> 18. A system according to Claim 17 further comprising a plurality of neural event waveform processors and wireless transmitters, and wherein the base station is configured to wirelessly receive the neural events that are transmitted by a plurality of the wireless transmitters and to further process the neural events that are wirelessly received.

As noted in the present application, for example at Page 6, lines 13-17:

> Some embodiments of the invention may also arise from recognition that in some conventional systems, multiple subjects may not easily and naturally interact and be recorded in the same closed environment. It may be desirable for subjects to interact with one another while being monitored so that the data reflects neurological activity in a realistic environment.

A central base station that can process events from multiple subjects is not described or suggested by Nicolelis et al., nor would such a central base station appear to be consistent with Nicolelis et al.'s desire to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*. Accordingly, Claim 18 is independently patentable.

Claims 31 and 34 recite that the waveforms exceed 1000 Hz, and Claims 32 and 35 recite that the waveforms exceed 1000 Hz and are less than 10,000 Hz. These waveforms are certainly not described or suggested in Nicolelis et al., and specifically appear to be filtered out in Nicolelis et al. Moreover, the mere existence of filters that can filter these waveforms, as may be described in DiLorenzo, would not render these claims obvious, because substitution of these filters into Nicolelis et al. would destroy the operability of Nicolelis et al., as was described above. Accordingly, these claims are also independently patentable.

Finally, Claims 33 and 36 recite that a plurality of single neuron action potentials are extracted and processed for a plurality of neurons with waveforms that exceed 500 Hz. As noted in the present application, for example at Page 10, lines 29-32:

> The device may allow segregation of signals from individual neurons as specific locations within the culture chamber that correspond to identified synaptic cellular events. Cultured neural networks may also be recordable with a WINE device.

Again, the extraction of multiple single neuron action potentials for multiple neurons is not described or suggested by Nicolelis et al., nor would such multiple single neuron action potentials appear to be consistent with Nicolelis et al.'s desire to provide an *"Intelligent Brain Pacemaker for Real-Time Monitoring and Controlling of Epileptic Seizures"*. Accordingly, these claims are also independently patentable.

Conclusion

Applicants again appreciate the continued thorough examination and the Examiner's analysis in the Advisory Action. Applicants have now shown, however, that substitution of DiLorenzo or any other high frequency waveform would appear to destroy the operability of the primary reference Nicolelis et al., and that the Examiner's analysis in the Advisory Action confirms that Nicolelis et al. teaches away from the substitution of such waveforms. Moreover, none of the cited references appear to describe or suggest the use of the same electrodes to capture electrical signals that are associated with a neuron and to stimulate the neuron itself, in a bidirectional manner. Finally, many of the dependent claims are separately patentable, and the withdrawn claims should be rejoined upon allowance of a generic claim. Accordingly, Applicants respectfully request entry of this Amendment, withdrawal of the outstanding rejections, and allowance of the present application. Applicants also request a telephone interview to discuss the above, so as to expedite the examination and allowance of this application.

Respectfully submitted,

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